What is claimed is:

1. A compound for inhibiting ALK according to formula I,

or a pharmaceutically acceptable salt, stereoisomer, prodrug or metabolite thereof, wherein,

A is a five- to ten-membered ring containing up to three heteroatoms; provided A is not a saturated alicyclic when  $X^2$  is =N-,  $X^3$  is -O-, and A is a pyridin-4-yl;

each of  $R^1$ ,  $R^2$  and  $R^3$  is independently selected from -H, halo, trihalomethyl, -CN, -NO<sub>2</sub>, -OR<sup>4</sup>, -N(R<sup>4</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>4</sup>, -SO<sub>2</sub>N(R<sup>4</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)N(R<sup>4</sup>)R<sup>4</sup>, -C(=O)R<sup>4</sup>, -C(=NR<sup>5</sup>)N(R<sup>4</sup>)R<sup>4</sup>, -C(=NR<sup>5</sup>)R<sup>4</sup>, -N(R<sup>4</sup>)SO<sub>2</sub>R<sup>4</sup>, -N(R<sup>4</sup>)C(O)R<sup>4</sup>, -NCO<sub>2</sub>R<sup>4</sup>, optionally substituted alkoxy, optionally substituted  $C_{1-6}$  alkyl, optionally substituted aryl, optionally substituted aryl  $C_{1-6}$  alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl  $C_{1-6}$  alkyl;

two adjacent of R<sup>1</sup>, together with the annular atoms to which they are attached, can form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to four of R<sup>10</sup>;

R<sup>2</sup> and R<sup>3</sup>, together with the annular atoms to which they are attached, can form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to five of R<sup>6</sup>;

each  $R^4$  is selected from -H, optionally substituted  $C_{1-6}$  alkyl, optionally substituted aryl, optionally substituted aryl  $C_{1-6}$  alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl  $C_{1-6}$  alkyl;

two of R<sup>4</sup>, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl, said optionally substituted five- to seven-membered heterocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P;

each  $R^5$  is selected from -H, -CN, -NO<sub>2</sub>, -OR<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, optionally substituted  $C_{1-6}$  alkyl, optionally substituted  $C_{2-6}$  alkenyl, and optionally substituted  $C_{2-6}$  alkynyl;

Y is =N- or = $C(R^8)$ -;

 $X^1$  and  $X^2$  are each independently either =N- or =C( $R^9$ )-;

 $X^3$  is selected from -N( $R^7$ )-, -O-, and -S-;

 $R^7$  is selected from -H, optionally substituted  $C_{1\text{-}6}$ alkyl, -SO<sub>2</sub>N( $R^4$ ) $R^4$ , -CO<sub>2</sub> $R^4$ , -C(=O)N( $R^4$ ) $R^4$ , -C(=N $R^5$ )N( $R^4$ ) $R^4$ , -C(=N $R^5$ ) $R^4$ , -C(=O) $R^4$ , optionally substituted alkoxy, optionally substituted aryl, optionally substituted aryl  $C_{1\text{-}6}$  alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl  $C_{1\text{-}6}$  alkyl;

each of  $R^6$ ,  $R^8$ ,  $R^9$  and  $R^{10}$  is independently selected from -H, halo, trihalomethyl, -CN, -NO<sub>2</sub>, -OR<sup>4</sup>, -N(R<sup>4</sup>)R<sup>4</sup>, -S(O)<sub>0-2</sub>R<sup>4</sup>, -SO<sub>2</sub>N(R<sup>4</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)N(R<sup>4</sup>)R<sup>4</sup>, -C(=NR<sup>5</sup>)N(R<sup>4</sup>)R<sup>4</sup>, -C(=NR<sup>5</sup>)R<sup>4</sup>, -N(R<sup>4</sup>)SO<sub>2</sub>R<sup>4</sup>, -N(R<sup>4</sup>)C(O)R<sup>4</sup>, -NCO<sub>2</sub>R<sup>4</sup>, -C(=O)R<sup>4</sup>, optionally substituted alkoxy, optionally substituted  $C_{1-6}$  alkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl  $C_{1-6}$  alkyl; provided when  $R^9$  is aryl, heteroaryl, -C(H)=C(H)R or -C(H)=NR, where R is an optionally substituted alkyl, cycloalkyl, heteroalicyclic, aryl, or heteroaryl, then Y is not =C(H)-; and

two adjacent of R<sup>6</sup>, together with the annular atoms to which they are attached, can form an optionally substituted five- to seven-membered ring containing up to two heteroatoms.

- 2. The compound according to claim 1, wherein  $R^2$  and  $R^3$ , together with the carbons to which they are attached, form a five- to six-membered ring containing up to two heteroatoms and optionally substituted with up to four of  $R^6$ .
- 3. The compound according to claim 2, wherein said five- to six-membered ring is an aryl or a heteroaryl.
- 4. The compound according to claim 3, wherein said five- to six-membered ring is phenyl or pyridyl.
- 5. The compound according to claim 4, of formula II,

6. The compound according to claim 5, wherein  $X^1$  is  $=C(R^9)$ -,  $X^2$  is =N-, and  $X^3$  is  $=N(R^7)$ -.

- 7. The compound according to claim 6, wherein Y is =N-.
- 8. The compound according to claim 7, wherein A is either a five- to ten-membered aryl or a five- to ten-membered heteroaryl containing up to three heteroatoms.
- 9. The compound according to claim 8, wherein A is either a five- or six-membered aryl or a five- or six-membered heteroaryl containing up to three heteroatoms.
- 10. The compound according to claim 9, wherein  $R^1$  is selected from -H, halo, trihalomethyl, -CN, -OR<sup>4</sup>, -N(R<sup>4</sup>)R<sup>4</sup>, -SO<sub>2</sub>N(R<sup>4</sup>)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)N(R<sup>4</sup>)R<sup>4</sup>, -C(=NR<sup>5</sup>)N(R<sup>4</sup>)R<sup>4</sup>, -C(=NR<sup>5</sup>)R<sup>4</sup>, -N(R<sup>4</sup>)SO<sub>2</sub>R<sup>4</sup>, -N(R<sup>4</sup>)C(O)R<sup>4</sup>, -NCO<sub>2</sub>R<sup>4</sup>, optionally substituted alkoxy, optionally substituted  $C_{1-6}$  alkyl, optionally substituted heterocyclyl  $C_{1-6}$  alkyl.
- 11. The compound according to claim 10, of formula III,

wherein at least one of R<sup>1</sup> is -OH.

- 12. The compound according to claim 11, wherein the compound is either a 3-(3H-pyrazolo[3,4-c]isoquinolin-5-yl)-phenol or a 4-(3H-pyrazolo[3,4-c]isoquinolin-5-yl)-phenol.
- 13. The compound according to claim 12, wherein  $R^9$  is selected from -H, trihalomethyl, optionally substituted alkoxy, optionally substituted  $C_{1-6}$  alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl  $C_{1-6}$  alkyl.
- 14. The compound according to claim 13, wherein  $R^6$  is selected from -H, halo, trihalomethyl, -CN,  $-OR^4$ ,  $-N(R^4)R^4$ ,  $-CO_2R^4$ ,  $-C(=O)N(R^4)R^4$ ,  $-N(R^4)SO_2R^4$ .

-N(R<sup>4</sup>)C(O)R<sup>4</sup>, -NCO<sub>2</sub>R<sup>4</sup>, -C(=O)R<sup>4</sup>, optionally substituted  $C_{1-6}$  alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl  $C_{1-6}$  alkyl, and a six- or seven-membered heteroalicyclic formed by two adjacent of R<sup>6</sup>, together with the annular atoms to which they are attached, said six- or seven-membered heteroalicyclic containing up to two heteroatoms.

- 15. The compound according to claim 14, wherein  $R^6$  is selected from -H, halo,  $-OR^4$ ,  $-N(R^4)R^4$ , optionally substituted  $C_{1-6}$  alkyl, optionally substituted heterocyclyl, optionally substituted heterocyclyl  $C_{1-6}$  alkyl, and a six-or seven-membered heteroalicyclic formed by two adjacent of  $R^6$ , together with the annular atoms to which they are attached, said six- or seven-membered heteroalicyclic containing up to two heteroatoms.
- 16. The compound according to claim 15, wherein at least one of  $R^6$  is optionally substituted  $C_{1-6}$  alkoxy.
- 17. The compound according to claim 16, wherein at least one of R<sup>1</sup> is halogen or methyl.
- 18. The compound according to claim 17, wherein  $R^9$  is selected from -H, trihalomethyl, and optionally substituted  $C_{1-6}$  alkyl.
- 19. The compound according to claim 15, wherein at least one of  $R^6$  is  $C_{1-6}$  alkoxy substituted with a heteroalicyclic.
- 20. The compound according to claim 19, wherein said heteroalicyclic is selected from the group consisting of dioxolanyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyrrolidinyl, morpholinyl, quinuclidinyl, tetrahydrofuryl, tetrahydropyranyl, thiamorpholinyl, thiamorpholinyl sulfoxide, 2,5-diaza-bicyclo[2.2.1]heptanyl, and thiamorpholinyl sulfone.
- 21. The compound according to claim 15, wherein at least one of  $R^6$  is  $C_{1-6}$  alkoxy substituted with at least one additional of an optionally substituted alkoxyl, an amino, an optionally substituted dialkylamino, and an optionally substituted monoalkylamino.

# 22. The compound according to claim 1, selected from Table 3.

Table 3

Entry	Name	Structure
1	7,8-bis(methyloxy)-5-phenyl-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinoline	
2	2-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	OH N N N N H
3	4-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO-ON-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
4	4-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-N,N-dimethylaniline	N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—
5	5-(4-fluorophenyl)-7,8- bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinoline	F—N=N-N

Table 3

Entry	Name	Structure
6	5-(4-nitrophenyl)-7,8- bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinoline	$O_2N$ $N$ $N$ $N$ $N$
7	4-[3-methyl-7,8-bis(methyloxy)-1-(phenylmethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
8	3-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO NO
9	4-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]benzene-1,2-diol	HO N N N N N N N N N N N N N N N N N N N
10	4-{7,8-bis(methyloxy)-1-[(4-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N

Table 3

Entry	Name	Structure
11	5-(1,3-benzodioxol-5-yl)-7,8- bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinoline	
12	4-(7,8-bis(methyloxy)-1-{[4- (methyloxy)phenyl]methyl}- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl)phenol	HO-ON-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
13	4-{7,8-bis(methyloxy)-1-[(2-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	HO N N N N N N N N N N N N N N N N N N N
14	4-{7,8-bis(methyloxy)-1-[(3-methylphenyl)methyl]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
15	4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N

Table 3

Entry	Name	Structure
16	2-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-6-fluorophenol	F OH N N N H
17	3-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-4-nitrophenol	H O O O O O O O O O O O O O O O O O O O
18	4-[7,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]benzoic acid	HO N N N
19	4-[7,8-bis(methyloxy)-1-(1-phenylethyl)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N = N = N = N = N = N = N = N = N = N =
20	4-[1-{[3,4- bis(methyloxy)phenyl]methyl}- 7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	N = N = N = N = N = N = N = N = N = N =

Table 3

Entry	Name	Structure
21	4-(7,8-bis(methyloxy)-1-{[3- (methyloxy)phenyl]methyl}- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl)phenol	HO N N N N N N N N N N N N N N N N N N N
22	4-[1-ethyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N = N
23	7,8-bis(methyloxy)-1- (phenylmethyl)-5-pyridin-4-yl- 3H-pyrazolo[3,4-c]isoquinoline	
24	4-[6,7,8-tris(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
25	4-[1-methyl-6,7,8- tris(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO-O-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N

Entry	Name	Structure
26	4-[8-(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
27	4-[7,8-bis(methyloxy)-1- (trifluoromethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————
28	4-[1-(1-methylethyl)-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N=NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
29	4-[7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————
30	4-[7-methyl-8-(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N N H

Table 3

Entry	Name	Structure
31	4-[1-methyl-6,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
32	4-[6,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————
33	4-[6,8-bis(methyloxy)-1- (phenylmethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	$HO \longrightarrow N \longrightarrow $
34	4-[6,7,8-tris(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO N N N N N N N N N N N N N N N N N N N
35	4-[1-methyl-7,8,9- tris(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————

	1	able 3
Entry	Name	Structure
36	4-[1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
37	2-methyl-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N
38	4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-2-(methyloxy)phenol	HO N N N N N N N N N N N N N N N N N N N
39	4-{1-methyl-8-(methyloxy)-7- [(2-morpholin-4-ylethyl)oxy]- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl}phenol	OH ON NO
40	2-(ethyloxy)-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO N N N H

Table 3

Entry	Name	Structure
41	2-chloro-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	CI N N N N N N N N N N N N N N N N N N N
42	2-fluoro-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N H
43	4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-2-nitrophenol	O=N+ HO N=N+ N=N+ N=N+ N=N+
44	2-bromo-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	Br NH
45	1-{[5-(4-hydroxyphenyl)-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-1-yl]methyl}pyrrolidin-2-one	HO

		able 3
Entry	Name	Structure
46	5-(4-fluorophenyl)-1-methyl- 7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinoline	F—————————————————————————————————————
47	2,6-dimethyl-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO N N N
48	5-[4-fluoro-3- (trifluoromethyl)phenyl]-1- methyl-7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinoline	F F H
49	5-(3-chloro-4-fluorophenyl)-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	F—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
50	5-(3,4-difluorophenyl)-1- methyl-7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinoline	F N N N N N N N N N N N N N N N N N N N

Table 3

Entry	Name	Structure
51	1-methyl-7,8-bis(methyloxy)-5- [3-(trifluoromethyl)phenyl]-3H- pyrazolo[3,4-c]isoquinoline	F F H
52	5-(4-fluoro-3-methylphenyl)-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	F—N=N=N
53	5-(3-bromo-4-fluorophenyl)-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	F N N N
54	4-{1-methyl-7-(methyloxy)-8- [(piperidin-4-ylmethyl)oxy]- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl}phenol	HN N NH
55	4-{1-methyl-8-(methyloxy)-7- [(piperidin-4-ylmethyl)oxy]- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl}phenol	OH OH NH

Table 3

Entry	Name	Structure
56	1-methyl-7,8-bis(methyloxy)-5- (3-methylphenyl)-3H- pyrazolo[3,4-c]isoquinoline	N N N N N N N N N N N N N N N N N N N
57	5-(3-bromophenyl)-1-methyl- 7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinoline	Br N N
58	4-[8-(ethyloxy)-1-methyl-7- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
59	4-[1-methyl-8,9-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO N N N N N N N N N N N N N N N N N N N
60	4-[7-(ethyloxy)-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N

Entry	Name	Structure
61	4-{1-methyl-8-(methyloxy)-9- [(piperidin-4-ylmethyl)oxy]- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl}phenol	HO N N N N N N N N N N N N N N N N N N N
62	4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-(1-methylethyl)phenol	HO N N N N N N N N N N N N N N N N N N N
63	2-ethyl-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N N N N N N N N N N N N N N N N N
64	4-(1-methyl-8-(methyloxy)-9- {[(1-methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	
65	4-(1-methyl-7-(methyloxy)-8- {[(1-methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	OH OH
66	4-[1,7-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO—N—N H

Table 3

Entry	Name	Structure
67	1,1-dimethylethyl 4-[5-(4-hydroxyphenyl)-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-1-yl]piperidine-1-carboxylate	HO NO
68	4-[7,8-bis(methyloxy)-1- piperidin-4-yl-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HZ N N N N N N N N N N N N N N N N N N N
69	2-chloro-4-[1-methyl-8,9- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	CI N N N N N N N N N N N N N N N N N N N
70	2-fluoro-4-[1-methyl-8,9- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N N N N N N N N N N N N N N N N N
71	2-methyl-4-[1-methyl-8,9- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO N N N N N N N N N N N N N N N N N N N
72	2-bromo-4-[1-methyl-8,9- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	Br O O

Table 3

Entur		Structure
Entry	Name	Structure
73	4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]benzonitrile	$N = \bigcup_{N=N}^{N-N} N$
74	N'-hydroxy-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzenecarboximidamide	$H_2N$ $N$ $N$ $N$ $N$ $N$
75	5-hydroxy-2-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-4H-pyran-4-one	HO N N N N
76	2-[(difluoromethyl)oxy]-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	F HO N N N N N N
77	5-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]pyridin-2-ol	HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N

Table 3

Entry		able 3
Entry	Name	Structure
78	4-[1,9-dimethyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
79	4-[6,9-difluoro-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO—F N=N=N=N=N=N=N=N=N=N=N=N=N=N=N=N=N=N=N=
80	2-bromo-4-{1-methyl-8- (methyloxy)-9-[(2-morpholin- 4-ylethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH NOH Br
81	2-chloro-4-{1-methyl-8- (methyloxy)-9-[(2-morpholin- 4-ylethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH N-NH N-NH N-OH
82	4-(7,8-bis(methyloxy)-1- {[(phenylmethyl)amino]methyl} }-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N = N + N + N + N + N + N + N + N + N +

Entry	Name	Structure
83	2,5-dimethyl-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	O $O$ $O$ $O$ $O$ $O$ $O$ $O$ $O$ $O$
84	2,3-dichloro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	CI CI N N N H
85	2,5-dichloro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	CI N N N N N N N N N N N N N N N N N N N
86	2,3-dimethyl-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO N N N N N N N N N N N N N N N N N N N
87	2-bromo-4-(1-methyl-8- (methyloxy)-9-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	HO Br N N N N N N N N N N N N N N N N N N N
88	2-chloro-4-(1-methyl-7- (methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N OH CI

Table 3

Entry	Name	Structure
89	4-[9-fluoro-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO—F N=N N-N H
90	4-(1-methyl-8-(methyloxy)-9- {[2-(methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	NH N
91	2-chloro-4-(1-methyl-8- (methyloxy)-9-{[(1- methylpiperidin-4- .yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	
92	4-[6-bromo-1,7-dimethyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	Br N N N N N N N N N N N N N N N N N N N
93	4-[6-fluoro-1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
94	4-[9-chloro-1,7-dimethyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO————————————————————————————————————

Table 3

Entry	Name	Structure
95	2-chloro-4-[8-{[(1- ethylpiperidin-4- yl)methyl]oxy}-1-methyl-7- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	N-NH N-OH CI
96	3-chloro-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO CI N N N N N N N N N N N N N N N N N N
97	4-(1-methyl-8,9-bis{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	HO N N N H
98	4-(1-methyl-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	HO—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N
99	2-chloro-4-(1-methyl-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	HO—N—NN N N N N N N N N N N N N N N N N N
100	2-bromo-4-(1-methyl-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	Br HO-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N

Table 3

Entry	Name	Structure
101	2-chloro-4-[1,7-dimethyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO N N N N N N N N N N N N N N N N N N N
102	2-bromo-4-[1,7-dimethyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	Br N N N N N N N N N N N N N N N N N N N
103	2-chloro-4-[1-methyl-8-({[1-(1-methylethyl)piperidin-4-yl]methyl}oxy)-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	H P C C
104	4-[9-bromo-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO————————————————————————————————————
105	4-[7-chloro-9-fluoro-1-methyl- 8-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————

Table 3

Entry	Name	Structure S
Entry	Ivame	Structure
106	4-[8-{[(1-acetylpiperidin-4-yl)methyl]oxy}-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	N-NH N-NH CI
107	4-[9-{[(1-acetylpiperidin-4-yl)methyl]oxy}-1-methyl-8-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-bromophenol	HO Br N N N N N N N N N N N N N N N N N N N
108	2-chloro-4-(1-methyl-9- (methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	OH CI
109	4-[7-fluoro-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO————————————————————————————————————
110	2-chloro-4-(1-methyl-8,9- bis{[2-(methyloxy)ethyl]oxy}- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl)phenol	CI N N H

Table 3

Entry	Name	Structure
111	2-bromo-4-(1-methyl-8,9-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	Br N N N N N N N N N N N N N N N N N N N
112	2-chloro-4-(1-methyl-8- (methyloxy)-9-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH NOH
113	2-bromo-4-(1-methyl-8- (methyloxy)-9-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N OH Br
114	3-fluoro-4-[1-methyl-7,8- bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	HO————————————————————————————————————
115	2-chloro-4-(1-methyl-7- (methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI N N N N N N N N N N N N N N N N N N N

Table 3

Entry	Name	Structure
116	2-bromo-4-(1-methyl-7- (methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	Br O O O O O O O O O O O O O O O O O O O
117	2-chloro-4-(1-methyl-7,8-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	
118	2-bromo-4-(1-methyl-7,8-bis{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	Br HO N=N N-N H
119	1-methyl-7,8-bis(methyloxy)-5- (1H-pyrazol-5-yl)-3H- pyrazolo[3,4-c]isoquinoline	HN, N
120	4-(6,9-difluoro-1-methyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	Z-Z-Z-M-M-M-M-M-M-M-M-M-M-M-M-M-M-M-M-M

Table 3

Entry	Name	Structure
121	2-chloro-5-fluoro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	CI HO F N N N N N N N
122	2-bromo-5-fluoro-4-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	Br HO F N N N N N N N N
123	4-[9-fluoro-1-methyl-7,8- bis(methyloxy)-3H- benzo[e]indazol-5-yl]phenol	F—OH NNNH
124	2-hydroxy-5-[1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]benzoic acid	HO—OH N—N N
125	3-fluoro-4-(1-methyl-7- (methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	OH F N N

Table 3

Entry	Name	Structure
126	4-(6,9-difluoro-1-methyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)-3-fluorophenol	OH F N HN N F
127	2-chloro-4-(6,9-difluoro-1- methyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI F F N N N N N N N N N N N N N N N N N
128	2-chloro-4-[8-(ethyloxy)-1- methyl-7-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	CI N N N N N N N N N N N N N N N N N N N
129	2-chloro-4-[6-chloro-1-methyl-7,8-bis(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	OH OH
130	3-fluoro-4-(1-methyl-9- (methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	OH F N N N N N N N N N N N N N N N N N N

F	Τ	able 5
Entry	Name	Structure
131	2-chloro-4-(1,7-dimethyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI N N N N H
132	3-fluoro-4-(6-fluoro-1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	OH F O O
133	2-chloro-4-[1-methyl-8-[(1-methylethyl)oxy]-7- (methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	CI N N N N N N N N N N N N N N N N N N N
134	2-chloro-4-{1-methyl-7- (methyloxy)-8-[(2- methylpropyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	NH NH CI
135	2-bromo-5-fluoro-4-(1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	H N F OH Br

Table 3

Entry	Name	Structure
136	4-[7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-2-chlorophenol	DH CI
137	4-[7,8-bis(methyloxy)-1- (trifluoromethyl)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]-2-chlorophenol	CI HO N=N N=N H
138	4-{7,8-bis(methyloxy)-1- [(methyloxy)methyl]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}-2-chlorophenol	HO NH
139	2-chloro-4-(1-methyl-3H- [1,3]dioxolo[4,5- g]pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI NH
140	2-chloro-4-(1-methyl-8,9- dihydro-3H-[1,4]dioxino[2,3- g]pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI N N N N N N N N N N N N N N N N N N N

Table 3

Entry	Name	Structure
141	2-chloro-4-(1-methyl-9,10- dihydro-3H,8H- [1,4]dioxepino[2,3- g]pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI N N N N N N N N N N N N N N N N N N N
142	2-chloro-4-[7- [(difluoromethyl)oxy]-1- methyl-8-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	CI HO N=N N
143	2-chloro-5-fluoro-4-(6-fluoro- 1-methyl-9-(methyloxy)-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N F OH CI
144	2-chloro-4-(6,9-difluoro-1- methyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)-5-fluorophenol	CI F O F N N N N N N N N N N N N N N N N N
145	2-chloro-4-(11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenol	HO N N N N N N N N N N N N N N N N N N N
146	2-chloro-5-fluoro-4-(11- methyl-2,3-dihydro-9H- [1,4]dioxino[2,3- f]pyrazolo[3,4-c]isoquinolin-7- yl)phenol	N-NH N F OH CI

Table 3

Entry	Name	Structure
147	2-chloro-4-[1-methyl-6,7,8- tris(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	
148	2-bromo-4-(6,9-difluoro-1- methyl-8-{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)-5-fluorophenol	Br F P N N N H
149	7-(3-chlorophenyl)-11-methyl- 2,3-dihydro-9H- [1,4]dioxino[2,3- f]pyrazolo[3,4-c]isoquinoline	N-NH N CI
150	2-chloro-5-fluoro-4-(6-fluoro- 1-methyl-8,9-dihydro-3H- [1,4]dioxino[2,3- g]pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI F N N N H
151	2-chloro-4-{1-methyl-7- (methyloxy)-8- [(tetrahydrofuran-2- ylmethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	H Z OH
152	2-chloro-4-{1-methyl-7- (methyloxy)-8-[(tetrahydro-2H- pyran-2-ylmethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH N-CI

Entry	Name	Structure
153	2-chloro-4-{1-methyl-7- (methyloxy)-8-[(2,2,2- trifluoroethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH N-NH CI
154	2-chloro-5-fluoro-4-[9-fluoro- 1-methyl-6,7,8-tris(methyloxy)- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl]phenol	CI O F N N N N N N N N N N N N N N N N N N
155	5-(3-chloro-4-hydroxyphenyl)- 6,9-difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	HO F OH
156	6,9-difluoro-5-(2-fluorophenyl)-1-methyl-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinoline	NNH F
157	2-chloro-4-{8- [(difluoromethyl)oxy]-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH F OH CI
158	2-chloro-4-(6,11-difluoro-1-methyl-8,9-dihydro-3H-[1,4]dioxino[2,3-g]pyrazolo[3,4-c]isoquinolin-5-yl)-5-fluorophenol	CI F F N N N N H

Entry	Name	Structure
159	4-(1-methyl-3H- benzo[e]indazol-5-yl)phenol	ОН
160	6-fluoro-7-(2-fluorophenyl)-11- methyl-2,3-dihydro-9H- [1,4]dioxino[2,3- f]pyrazolo[3,4-c]isoquinoline	N-NH N F
161	2-chloro-4-{1-methyl-7- (methyloxy)-8-[(tetrahydro-2H- pyran-4-ylmethyl)oxy]-3H- pyrazolo[3,4-c]isoquinolin-5- yl}phenol	N-NH N-OH CI
162	2-chloro-4-[8-{[2- (ethyloxy)ethyl]oxy}-1-methyl- 7-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	CI NH
163	N-[4-(6-fluoro-11-methyl-2,3-dihydro-9H-[1,4]dioxino[2,3-f]pyrazolo[3,4-c]isoquinolin-7-yl)phenyl]acetamide	N-NH N N N
164	3-fluoro-4-(6-fluoro-11-methyl- 2,3-dihydro-9H- [1,4]dioxino[2,3- f]pyrazolo[3,4-c]isoquinolin-7- yl)phenol	N-NH NH N

Table 3

Entry	Name	Structure
165	2-chloro-5-fluoro-4-(6-fluoro- 11-methyl-2,3-dihydro-9H- [1,4]dioxino[2,3- f]pyrazolo[3,4-c]isoquinolin-7- yl)phenol	DH CO
166	2-chloro-4-[8-(cyclopentyloxy)- 1-methyl-7-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	N-NH N CI
167	2-chloro-4-(1-methyl-7-(1-methylethyl)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	CI N N N H
168	2-chloro-4-[9-ethyl-1-methyl-8- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	HO N N N N N N N N N N N N N N N N N N N
169	2-chloro-4-(6,9-difluoro-1-methyl-8-{[(1-methylpiperidin-4-yl)methyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	NH NH CI
170	5-(3-chloro-4-hydroxyphenyl)- 8-fluoro-1-methyl-7- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-6-ol	HO————————————————————————————————————

Entry	Name	Structure
171	2-chloro-4-(6-fluoro-1-methyl- 7-(methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N-NH N-NH N-NH OH CI
172	2-chloro-4-(6-fluoro-1-methyl- 8,9-bis{[2- (methyloxy)ethyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	CI F N N N N N N N N N N N N N N N N N N
173	5-[3-chloro-4- (methyloxy)phenyl]-6-fluoro-1- methyl-7-(methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinoline	N NH N CI O F O O
174	5-[3-chloro-4- (methyloxy)phenyl]-8-fluoro-1- methyl-7-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-6-ol	HO————————————————————————————————————
175	5-[3-chloro-4- (methyloxy)phenyl]-1-methyl- 7,8-bis(methyloxy)-3H- pyrazolo[3,4-c]isoquinoline	

Entry	Name	Structure
176	2-chloro-4-{6-fluoro-1-methyl-7-(methyloxy)-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	H P OH OH
177	2-chloro-4-[8-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-7-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	NH N
178	2-chloro-4-[8-{[2- (diethylamino)ethyl]oxy}-6- fluoro-1-methyl-7-(methyloxy)- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl]phenol	N-NH OH OH
179	2-chloro-4-(6-fluoro-1-methyl-7-(methyloxy)-8-{[2-(methyloxy)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	CI F N N N N N N N N N N N N N N N N N N
180	6,9-difluoro-5-furan-3-yl-1- methyl-3H-pyrazolo[3,4- c]isoquinolin-8-ol	HN P
181	6,9-difluoro-5-furan-2-yl-1- methyl-3H-pyrazolo[3,4- c]isoquinolin-8-ol	H S S S S S S S S S S S S S S S S S S S

Entry	Name	Structure
182	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N O F OH CI
183	2-bromo-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N O F O Br
184	2-chloro-5-fluoro-4-(6-fluoro- 1-methyl-9-(methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH N-NH N-NH N-NH N-NH N-NH N-NH N-NH
185	4-(6-fluoro-1-methyl-9- (methyloxy)-8-{[(1- methylpiperidin-4- yl)methyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)-2-methylphenol	N-NH N-NH N-NH N-NH N-NH
186	2-chloro-4-{6,9-difluoro-1-methyl-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N-NH N-NH N-NH N-NH N-NH N-NH N-NH N-NH
187	2-chloro-4-(8-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	N-NH N-NH N-NH N-NH N-NH N-NH N-OH CI

Table 3

Entry	Name	Structure
188	2-chloro-4-(8-{[2- (diethylamino)ethyl]oxy}-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N-NH F OH CI
189	4-(6,9-difluoro-8-hydroxy-1- methyl-3H-pyrazolo[3,4- c]isoquinolin-5-yl)-N- hydroxybenzenecarboximidami de	HN N N N N N N N N N N N N N N N N N N
190	3-(6,9-difluoro-8-hydroxy-1- methyl-3H-pyrazolo[3,4- c]isoquinolin-5-yl)-N- hydroxybenzenecarboximidami de	HN F F N N N N N N N H
191	6,9-difluoro-5-(1H-indol-5-yl)- 1-methyl-3H-pyrazolo[3,4- c]isoquinolin-8-ol	HN N N N N N N N N N N N N N N N N N N
192	5-(1H-benzimidazol-6-yl)-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	OH F N N N
193	5-(4-aminophenyl)-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	H <sub>2</sub> N————————————————————————————————————

Entry	Name	Structure
194	2-chloro-4-(6-fluoro-1-methyl-7-(methyloxy)-8-{[2-(4-methylpiperazin-1-yl)ethyl]oxy}-3H-pyrazolo[3,4-c]isoquinolin-5-yl)phenol	N-NH N N N O F CI
195	5-(2-amino-1,3-thiazol-5-yl)- 6,9-difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	N-NH N S NH <sub>2</sub>
196	2-chloro-4-[8-{[2-(4- ethylpiperazin-1-yl)ethyl]oxy}- 6-fluoro-1-methyl-9- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]phenol	OH CI F N N N
197	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[2-(4- methylpiperazin-1- yl)ethyl]oxy}-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N-NH N-NH N-NH N-OH CI
198	5-(6-aminopyridin-3-yl)-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	H <sub>2</sub> N—N=NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
199	5-(5-amino-2-thienyl)-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	H <sub>2</sub> N S N N N N N N N N N N N N N N N N N N

Table 3

Entry	Name	Structure
200	2-chloro-4-[8-{[3-(4- ethylpiperazin-1- yl)propyl]oxy}-6-fluoro-1- methyl-9-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	N NH N N N N N N N N N N N N N N N N N
201	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[3-(4- methylpiperazin-1- yl)propyl]oxy}-3H- pyrazolo[3,4-c]isoquinolin-5- yl)phenol	N NH N CI OH
202	6,9-difluoro-5-(1H-indol-6-yl)- 1-methyl-3H-pyrazolo[3,4- c]isoquinolin-8-ol	N-NH N HO F
203	N-[5-(6,9-difluoro-8-hydroxy- 1-methyl-3H-pyrazolo[3,4- c]isoquinolin-5-yl)-1,3-thiazol- 2-yl]acetamide	OH F S N N N N N N N N N N N N N N N N N N
204	5-(3-chlorophenyl)-8-{[2-(4-ethylpiperazin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinoline	
205	5-(3-aminophenyl)-6,9- difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	N-NH N N NH <sub>2</sub>



E 4	<u> </u>	able 5
Entry	Name	Structure
206	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-morpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N-NH N O N O H CI
207	4-[8-({2- [butyl(ethyl)amino]ethyl}oxy)- 6-fluoro-1-methyl-9- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]-2- chlorophenol	H Z OH
208	4-[8-{[(2R)-2-amino-3-methylbutyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	H <sub>2</sub> N OH CI
209	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[2-(1- methylpiperidin-4- yl)ethyl]oxy}-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N-NH N O F CI
210	2-chloro-4-[8-{[(1- ethylpiperidin-4- yl)methyl]oxy}-6-fluoro-1- methyl-9-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	N O H CI
211	5-(2-amino-1,3-thiazol-4-yl)- 6,9-difluoro-1-methyl-3H- pyrazolo[3,4-c]isoquinolin-8-ol	H <sub>2</sub> N N N N N N N N N N N N N N N N N N N

Table 3

Entry	Name	Structure
212	5-(5-amino-1,3,4-thiadiazol-2-yl)-6,9-difluoro-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	F HO
213	4-[8-{[(2R)-2-amino-3,3-dimethylbutyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	CI F O NH2
214	2-chloro-4-[6-fluoro-1-methyl-9-(methyloxy)-8-({2-[4-(2-methylpropyl)piperazin-1-yl]ethyl}oxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	OH CI N N N N N N N N N N N N N
215	2-chloro-4-[8-{[2-(5-ethyl-2,5-diazabicyclo[2.2.1]hept-2-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N-NH N-NH CI
216	2-chloro-4-[6-fluoro-1-methyl- 8-({2-[4-(1- methylethyl)piperazin-1- yl]ethyl}oxy)-9-(methyloxy)- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl]phenol	OH CI F NN NN

Table 3

Entry	Name	Structure
217	4-[8-{[2-(3-amino-8-azabicyclo[3.2.1]oct-8-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	H <sub>2</sub> N O F OH
218	2-chloro-4-[8-{[2-(1-ethylpiperidin-4-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	OH CI F N N N N N N N N N N N N N N N N N N
219	2-chloro-4-[8-{[2- (diethylamino)ethyl]oxy}-6- fluoro-1-methyl-9-(methyloxy)- 3H-pyrazolo[3,4-c]isoquinolin- 5-yl]phenol	N-NH N-NH N-NH OH CI
220	2-chloro-5-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-pyrrolidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N NH
221	6,9-difluoro-5-(2-imino-3-methyl-2,3-dihydro-1,3-thiazol-5-yl)-1-methyl-3H-pyrazolo[3,4-c]isoquinolin-8-ol	H S NH F HO

Entry	Name	Structure
222	6,9-difluoro-1-methyl-5-(1,3- thiazol-5-yl)-3H-pyrazolo[3,4- c]isoquinolin-8-ol	F——F
223	2-chloro-4-[6-fluoro-1-methyl-8-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	OH CI F NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN
224	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(3-pyrrolidin-1-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N-NH N O F O CI
225	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(3-piperidin-1-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N-NH NO F CI
226	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(3-morpholin-4-ylpropyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	
227	2-chloro-4-[8-({2-[[2-(dimethylamino)ethyl](methyl) amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N-NH N-NH N-NH N-N-OH CI

Table 3

	T	able 5
Entry	Name	Structure
228	2-chloro-4-[8-({2-[[2- (diethylamino)ethyl](methyl)a mino]ethyl}oxy)-6-fluoro-1- methyl-9-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	OH CI F N
229	2-chloro-4-[8-({2-[[2- (dimethylamino)ethyl](ethyl)a mino]ethyl}oxy)-6-fluoro-1- methyl-9-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	OH CI P N N N N N N N N N N N N N N N N N N
230	4-[8-[(2-{bis[3- (dimethylamino)propyl]amino} ethyl)oxy]-6-fluoro-1-methyl-9- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]-2- chlorophenol	OH CI N N N N N N N N N N N N N N N N N N
231	2-chloro-4-[6-fluoro-1-methyl-8-({2-[methyl(1-methylpyrrolidin-3-yl)amino]ethyl}oxy)-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N-NH N-NH N-NH N-NH N-OH
232	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-{(2S)-2-[(methyloxy)methyl]pyrrolidin-1-yl}ethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	HO F P P P P P P P P P P P P P P P P P P

Table 3

	T	able 5
Entry	Name	Structure
233	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[2-(4- pyrrolidin-1-ylpiperidin-1- yl)ethyl]oxy}-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N-NH NO F OH
234	2-chloro-4-[8-{[2-(4- cyclohexylpiperazin-1- yl)ethyl]oxy}-6-fluoro-1- methyl-9-(methyloxy)-3H- pyrazolo[3,4-c]isoquinolin-5- yl]phenol	N-NH NOH F OH
235	2-[4-(2-{[5-(3-chloro-4-hydroxyphenyl)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-8-yl]oxy}ethyl)piperazin-1-yl]-N-(1-methylethyl)acetamide	OH CI NO
236	4-[8-{[2-(1,4'-bipiperidin-1'-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	HO N N N N N N N N N N N N N N N N N N N
237	2-chloro-4-[6-fluoro-1-methyl-8-{[2-(4-methyl-1,4-diazepan-1-yl)ethyl]oxy}-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	HO————————————————————————————————————

Table 3

	Table 5		
Entry	Name	Structure	
238	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[2-(4- pyridin-2-ylpiperazin-1- yl)ethyl]oxy}-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N-NH N-NH N-NH CI	
239	2-chloro-4-[8-{[2-(2,6-dimethylmorpholin-4-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	OH CI F NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	
240	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-thiomorpholin-4-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	S N O H CI	
241	2-chloro-4-[8-{[2-(2,6-dimethylpiperidin-1-yl)ethyl]oxy}-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]phenol	N-NH N O F O CI	
242	2-chloro-4-(6-fluoro-1-methyl- 9-(methyloxy)-8-{[2- (octahydroquinolin-1(2H)- yl)ethyl]oxy}-3H-pyrazolo[3,4- c]isoquinolin-5-yl)phenol	N-NH NOH FOH	

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Table 3

Table 5		
Entry	Name	Structure
243	4-[8-({2-[bis(1-methylethyl)amino]ethyl}oxy)-6-fluoro-1-methyl-9-(methyloxy)-3H-pyrazolo[3,4-c]isoquinolin-5-yl]-2-chlorophenol	N-NH N O F OH
244	4-[8-[(2-{bis[2- (methyloxy)ethyl]amino}ethyl) oxy]-6-fluoro-1-methyl-9- (methyloxy)-3H-pyrazolo[3,4- c]isoquinolin-5-yl]-2- chlorophenol	OH CI N N N N N N N N N N N N N N N N N N
245	2-chloro-4-{6-fluoro-1-methyl-9-(methyloxy)-8-[(2-piperidin-1-ylethyl)oxy]-3H-pyrazolo[3,4-c]isoquinolin-5-yl}phenol	N-NH NOH F OH
246	6,9-difluoro-1-methyl-5-(1- oxidopyridin-4-yl)-3H- pyrazolo[3,4-c]isoquinolin-8-ol	O-N P N N N N N N N N N N N N N N N N N N

- 23. A pharmaceutical composition comprising the compound according to any one of claims 1 22 and a pharmaceutically acceptable carrier.
- 24. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 23.
- 25. A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of the compound or the pharmaceutical composition according to any of claims 1 23.

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26. The method according to claim 25, wherein the kinase is ALK.

- 27. The method according to claim 26, wherein modulating the *in vivo* activity of ALK comprises inhibition of ALK.
- 28. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of the compound or the pharmaceutical composition as described in any one of claims 1 23.
- 29. A method of screening for modulators of ALK, the method comprising combining a compound according to any one of claims 1 22, and at least one candidate agent and determining the effect of the candidate agent on the ALK activity.
- 30. A method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of a composition comprising a compound according any one of claims 1 22 to a cell or a plurality of cells.